Tetrahedron Letters No. 15, pp 1409 - 1412, 1972. Pergamon Press. Printed in Great Britain.

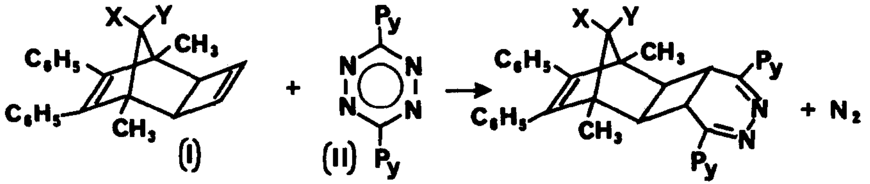
ORBITAL INTERACTIONS THROUGH SPACE (II). A PERTURBATIONAL MO TREATMENT OF SUBSTITUENT EFFECTS ON A $[_{\pi}4_s + _{\pi}2_s]$ PERICYCLIC REACTION.

Michael N. Paddon-Row

Department of Chemistry, Australian National University,
Canberra, A.C.T. 2600 Australia

(Received in UK 21 February 1972; accepted for publication 2 March 1972)

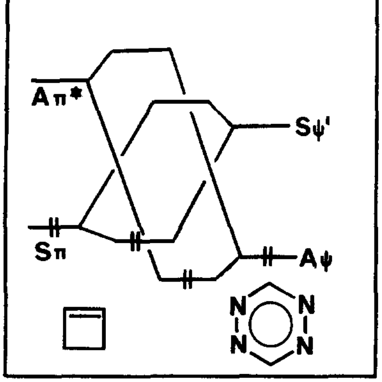
In the previous letter we reported the effect of substituents on the rate of $[_{\pi}4_S + _{\pi}2_S]$ reactions of the cyclobutene (I) with 3,6-di(2'pyridyl)-*s*-tetrazine (II), a diene having inverse electron demand. Whereas the 9-methoxy-compound [Ia] reacts faster than the unsubstituted compound (Ib) by a factor of *ca* 30, the keto-compound [Ic] was slower by a similar amount. It is the purpose of this letter to rationalise these effects, using perturbation theory, in terms of orbital interactions through space and to make some predictions concerning the effects of other substituents. We assume that $[_{\pi}4_s + _{\pi}2_s]$ reactions are frontier controlled(*1*) and that charge control(*2*), is of secondary importance. The dominant interactions then, are those between the highest occupied (HOMO) and lowest unoccupied (LUMO) molecular orbitals of the diene and dienophile and their symmetry allowed combinations are represented in Figure 1.

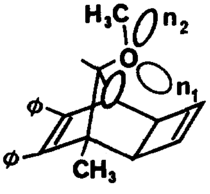


a) X = H ; Y = OCH₃ b) X = Y = H c) X = Y = O

As the diene and dienophile approach one another the HOMO's of both molecules are lowered in energy and the activated complex is stabilized. The rate of reaction will become faster as this stabilization energy dE becomes more negative. Now $dE = dE_{\psi} + dE_{\pi}$ where dE_{π} is the stabilization energy of the πMO of cyclobutene and dE_{ψ} is the stabilization energy of the HOMO(*4*) of tetrazine.

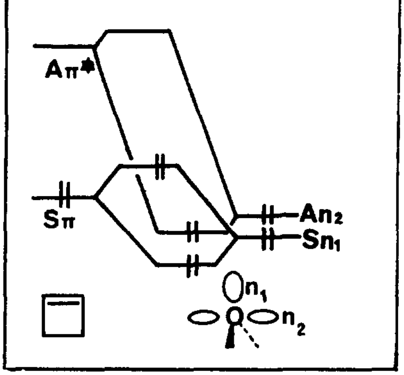
FIG.1





(III)

FIG. 2



The magnitudes of dE_Π and dE_ψ vary inversely with the energy difference between the interacting MO's. Application of 1st order perturbation theory(*3*) to *s*-tetrazine reveals that both ψ and ψ' are depressed in energy with respect to the corresponding MO's of benzene. The energy separation between Π and ψ' is therefore less than between Π^* and ψ in which case dE_Π becomes the major term in determining(*4*) the magnitude of dE. A substituent in the 9-position of compound (I) which elevates the ΠMO energy of the cyclobutene reduces the energy gap between Π and ψ' thereby making dE more negative. An *increase* in rate of reaction is predicted. Likewise a substituent which *depresses* the ΠMO energy will cause a *decrease* in rate.†

Consider the methoxy-compound (Ia). A consideration of steric factors indicates that the most stable rotamer is (III); the conformation in which the $O\text{-}CH_3$ bond is contained in the molecular plane of symmetry. The two non bonding atomic orbitals (NBAO), n_1 and n_2, of the oxygen atom may enter into symmetry allowed interactions with the Π and Π^* MO's of the cyclobutene double bond resp. (Fig. 2) *(14)*. As a consequence of this interaction through space the energy of the ΠMO, E_Π, is perturbed and the new energy is given to the second order(*3*) by

$$E'_\Pi = E_\Pi + \frac{(H_{\Pi n_1})^2}{E_\Pi - E_{n_1}} \qquad H_{\Pi n_1} = \left\langle \psi_\Pi \middle| P \middle| \psi_{n_1} \right\rangle$$

where E_{n_1} is the energy of the NBAO n_1 of oxygen and $H_{\Pi n_1}$ is the matrix element of the perturbation. This equation applies to the non-degenerate case. If $E_{n_1} < E_\Pi$ then $E'_\Pi > E_\Pi$ and the rate of reaction should increase. If we make the approximation [Koopmans' theorem(*5*)] that one electron orbital energies are

---

† These predictions relate only to electron deficient diene systems.

given by the negative of their ionization potentials (I.P.) then E_{Π} for cyclobutene is -9.43 ev(*6*). Substituents having NBAO's such that $E_{n_1} < E_{\Pi}$ are methoxy [I.P. Me$\underline{O}$Et = 9.81 ev(*7*)], fluoro [I.P. Me$\underline{F}$ 12.74 ev(*8*)], chloro [I.P. Me$\underline{Cl}$ = 11.28 ev(*8*)], bromo [I.P. iPr$\underline{Br}$ = 10.27 ev(*9*)] and iodo [I.P. iPr$\underline{I}$ = 9.47 ev(*9*)].

If $E_{n_1} > E_{\Pi}$ then $E'_{\Pi} < E_{\Pi}$ and the rate of reaction should decrease. Two substituents which fall into this category are amines [I.P. $Me_3\underline{N}$ = 7.82 ev(*7*)] and sulphides [I.P. $Me_2\underline{S}$ = 8.67 ev(*10*)]. The implication that an amine substituent should retard the rate of reaction of (I) with dienes having inverse electron demand is extraordinary and two points must be made.

(a) We have assumed that the significant change in the ΠMO energy of the cyclobutene is due to orbital interactions through space and that other effects which could, for example, alter the values of the coulomb integrals of the double bond carbon atoms, are minimal. The fairly large distance directly separating the substituent from the double bond (*ca* 2.2Å) and the number of intervening sigma bonds (four) justify this assumption. Our treatment is inapplicable to such cases as enamines where the nitrogen atom is directly attached to the double bond. Indeed it has been demonstrated(*11*) that the ΠMO energy is *raised* (compared with ethylene) for certain enamines.

(b) Although interaction between the NBAO of nitrogen (n_1) with the ΠMO of cyclobutene results in a depression in energy of the latter, the energy of the MO resembling n_1 is raised. Since this MO contains only a small admixture of Π it should be of minor importance(*12*) in determining the magnitude of dE.

For the keto-compound (Ic) the ΠMO of the cyclobutene may interact with both the Π_{CO} and Π^*_{CO} MO's of the carbonyl group, the change in energy being given by

$$E'_{\Pi} - E_{\Pi} = \frac{H^2_{\Pi\Pi_{CO}}}{E_{\Pi} - E_{\Pi_{CO}}} + \frac{H^2_{\Pi\Pi^*_{CO}}}{E_{\Pi} - E_{\Pi^*CO}}$$

The first term is positive and the second is negative. Although HMO theory would be unreliable in predicting the outcome of this interaction it has been shown(*13*) using photoelectron spectroscopy that for 7-norbornenone the ΠMO energy is lowered (i.e. the second term in the expression is dominant). The diminished reactivity of (Ic) is thereby explained.

Reactions of compound (I) with electron rich dienes, yet to be investigated, may be analysed similarly. In this case dE_ψ is the major term(*4*) and substituents having NBAO's (n_2; (III)) of the appropriate symmetry which *lower* the Π^* energy will cause an increase in reactivity of (I). However these substituents (oxygen, Halogens) *raise* the Π^* level (Figure 2) and therefore a small decrease in rate is expected. Amine and carbonyl substituents which lack an orbital of the appropriate symmetry will not, to the first approximation, affect the Π^* level. Their effect on dE_Π has been discussed (*v.s.*) and a small decrease in rate is predicted.

REFERENCES

(*1*) K. Fukui, *Bull. Chem. Soc. Japan,* 39, 498 (1966).

(*2*) R.F. Hudson and G. Klopman, *Tetrahedron Letters,* 1103 (1967).

(3) M.J.S. Dewar, "The Molecular Orbital Theory of Organic Chemistry", McGraw-Hill, New York, 1969.

(*4*) R. Sustmann, *Tetrahedron Letters,* 2717, 2721 (1971).

(*5*) T. Koopmans, *Physica,* 1, 104 (1933).

(*6*) P. Bischof and E. Heilbronner, *Helv. Chim. Acta,* 53, 1677 (1970).

(*7*) D.W. Turner in "Advances in Physical Organic Chemistry", V. Gold Ed., Academic Press, New York, *Vol. 4,* 1966.

(*8*) D.W. Turner, C. Baker, A.D. Baker, and C.R. Brundle, "Molecular Photoelectron Spectroscopy", Wiley Interscience, New York, 1970.

(*9*) F. Brogli and E. Heilbronner, *Helv. Chim. Acta,* 54, 1423 (1971).

(*10*) H. Bock and G. Wagner, *Tetrahedron Letters,* 3713 (1971)

(*11*) B. Cetinkaya, G.H. King, S.S. Krishnamurthy, M.F. Lappert and J.B. Pedley, *Chem. Comm.,* 1370 (1971).

(*12*) We believe that attack of the diene on (I) occurs in an *exo*-manner (Preceding letter). Interactions between the NBAO of the substituent and the MO's of the diene will be negligible.

(*13*) D. Chadwick, D.C. Frost and L. Weiler, *J. Amer. Chem. Soc.,* 93, 4962 (1971).

(*14*) The presence of "s" character in n_1 places it below n_2 in energy. The sequence of the first two perturbed orbitals is determined essentially by the difference in energy between the interacting orbitals (the matrix elements $H_{\Pi n_1}$ and $H_{\Pi^* n_2}$ are small and nearly equal[3]).